

# THE STEREOCHEMISTRY OF THE DECOMPOSITION OF 1-PYRAZOLINES

By  
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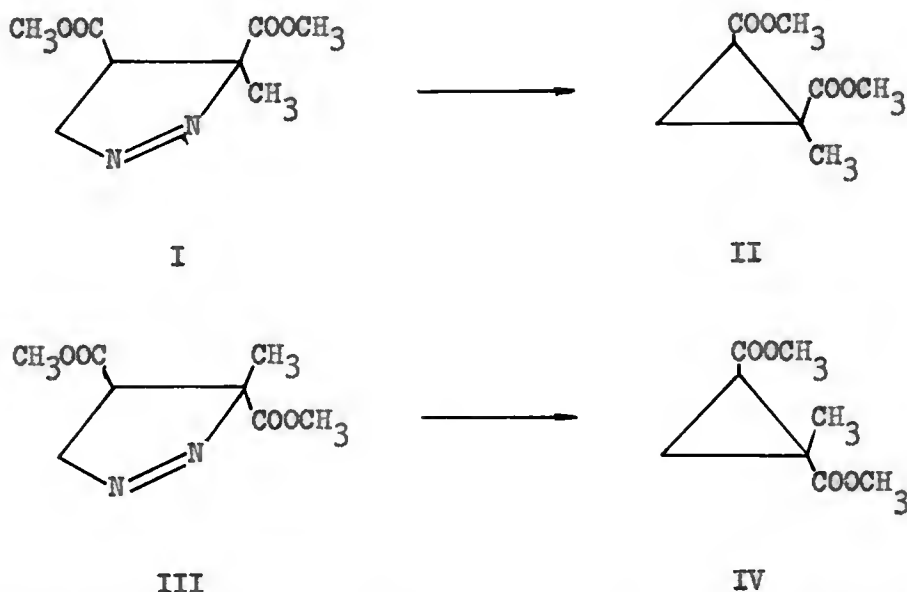
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## I. INTRODUCTION

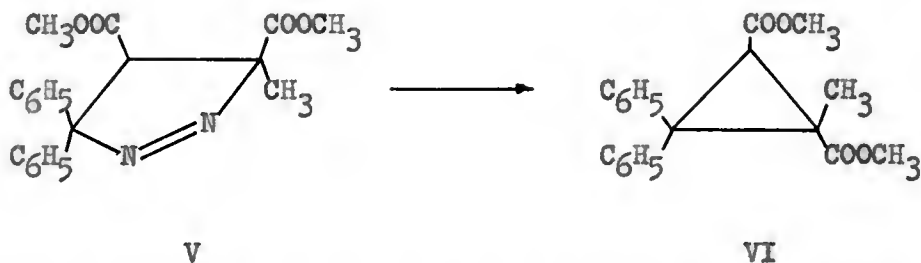
It has been generally assumed that the decomposition of 1-pyrazolines occurs stereospecifically.<sup>1,2</sup> This assumption has been based only on the examination of 1-pyrazolines with methylene groups adjacent to the nitrogen,<sup>3</sup> e.g.



It is rather difficult to make this observation consistent with either an ionic or a diradical mechanism for the decomposition of 1-pyrazolines unless it is assumed that the ring-closure to cyclopropane occurs more rapidly than rotation around the single bonds.

Van Alphen's work<sup>4</sup> on the decomposition of a 1-pyrazoline with two phenyl groups on the C-5 atom confirmed this assumption. According to

his results, the decomposition of 3-methyl-cis-3,4-dicarbomethoxy-5,5-diphenyl-1-pyrazoline (V) yielded, rather than the anticipated cis-isomer, exclusively 1-methyl-trans-1,2-dicarbomethoxy-3,3-diphenylcyclopropane (VI), indicating a lack of stereospecificity in this reaction.

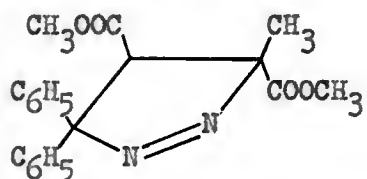


From a consideration of the kind of the substituents on the C-5 atom of the afore-mentioned 1-pyrazolines, it appeared that the competition between ring-closure and rotation is dependent upon the stability of the decomposition intermediate.

In an attempt to rationalize the stereochemistry of the decomposition of certain 5-phenyl-2-pyrazolines, Jones has assumed that 5-phenyl-1-pyrazolines decompose stereoselectively.<sup>5,6</sup> Inherent in this assumption was the assumption that a single phenyl on the C-5 atom of the 1-pyrazoline would not have enough stabilizing effect on the decomposition intermediate to allow free rotation around the single bonds. However, in view of the observations of van Alphen, it became apparent that the validity of these assumptions might well be questioned. Thus, the purpose of this project was to test the validity of these assumptions. The approach employed was an examination of the stereochemistry of the decomposition of the isomeric 3-methyl-3,4-dicarbomethoxy-5-phenyl-1-pyrazolines.

## II. RESULTS AND DISCUSSIONS

At the time when this work was begun, van Alphen's result<sup>4</sup> was the only known example of a non-stereospecific decomposition of a 1-pyrazoline. His work was repeated and compared with the decomposition of the isomeric 3-methyl-trans-3,4-dicarbomethoxy-5,5-diphenyl-1-pyrazoline (VII), an addition product of diphenyldiazomethane and dimethyl mesaconate. The purpose of the comparison was two-fold. One was to ensure that the addition of diphenyldiazomethane to dimethyl citraconate was in a cis-fashion so that the stereochemistry of the 1-pyrazoline (V) prepared by van Alphen was as claimed. The other was to provide further proof that the decomposition of van Alphen's 1-pyrazoline (V) was non-stereospecific. If the decomposition of these pyrazolines (V) and (VII) were non-stereospecific, both pyrazolines should yield the same product, namely, 1-methyl-trans-1-2-dicarbomethoxy-3,3-diphenylcyclopropane (VI).

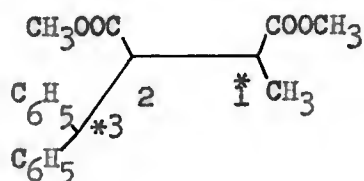


VII

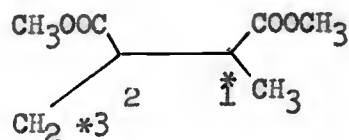
This has been found to be the case. When cis-pyrazoline (V, m.p. 124°C., dec.) and trans-pyrazoline (VII, m.p. 103°C., dec.) were decomposed at their respective melting temperatures, both pyrazolines yielded

nearly one hundred percent yields of trans-cyclopropane. The identity of both decomposition products was confirmed by infrared spectra and mixed melting points.

The non-stereospecificity of the decomposition of pyrazolines (V) and (VII) may be explained as due to the stabilizing effect of the two phenyl groups on the C-3 atom of the decomposition intermediate (VIII, either ionic or free radical). The life-time of the intermediate could thus become sufficiently long to permit free rotation around the single bonds before the ring-closure could occur.



VIII

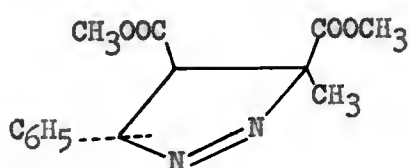


IX

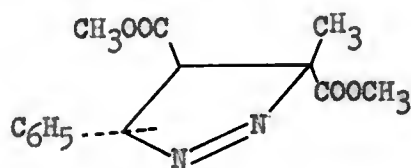
On the other hand, the decomposition of 3-methyl-cis-3,4-dicarbo-methoxy-1-pyrazoline (I) and its isomeric trans-pyrazoline (II) have been found to be stereospecific.<sup>3</sup> In this case, the ring-closure of the intermediate (IX) to cyclopropane apparently occurs more rapidly than rotation around the single bonds. This is reasonable in view of the system investigated since either a primary carbonium ion or primary free radical would be expected to be extremely reactive.

The afore-mentioned two extreme results aroused interest in an investigation of the analogous 1-pyrazoline with one phenyl group on the C-5 atom. Thus, although it has been suggested that a 5-phenyl-1-pyrazoline probably decomposes stereoselectively,<sup>5,6</sup> this has not been previously demonstrated.

For this purpose the stereochemistry of the decomposition of 3-methyl-cis-3,4-dicarbomethoxy-5-phenyl-1-pyrazoline (X) and the isomeric 3-methyl-trans-3,4-dicarbomethoxy-5-phenyl-1-pyrazoline (XII) were investigated. The two pyrazolines X and XII were prepared from the addition reactions of phenyldiazomethane with dimethyl citraconate and dimethyl mesaconate respectively. (At this stage, the configuration of the phenyl group can not be assigned. It will be determined later on.)



X

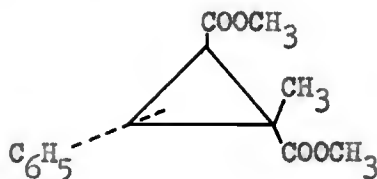


XII

The decomposition of the trans-1-pyrazoline (XII) was carried out at 180-185°C. The analysis of the decomposition product by gas chromatography using an 18 ft. column of 30-60 mesh Tide in a Perkin Elmer Model 154-B Fracometer at 190°C. at an internal pressure of 25 p.s.i. revealed the presence of a single cyclopropane peak with a retention time of 12.7 min.

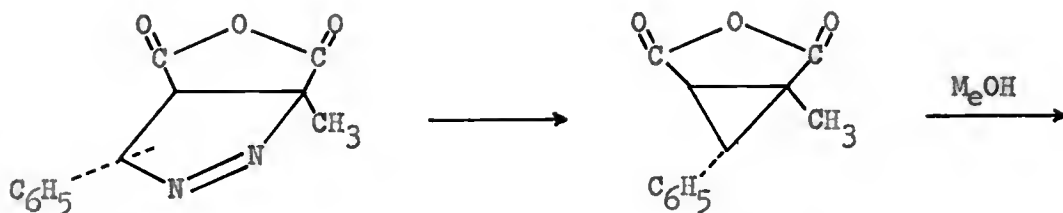
The cyclopropane (XIII) was isolated from the distillate of the crude reaction mixture of the trans-1-pyrazoline (XII) by liquid phase chromatography and was confirmed by an elementary analysis and  $\text{KMnO}_4$  test. In order to gain some knowledge of the configurations of the two carbomethoxy groups, the cyclopropane was hydrolyzed under alkaline conditions and an attempt was made to close the resultant di-acid to an anhydride by heating the di-acid at 200-230°C. and 30 mm.Hg. Only unchanged acid sublimed, indicating that the two carbomethoxy groups in the cyclopropane were trans. The possibility of the isomerization of the di-acid during saponification

was eliminated by converting the di-acid to the original cyclopropane by methylation with diazomethane.



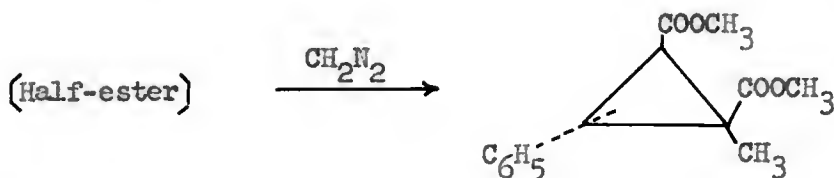
XIII

When the cis-1-pyrazoline (X) was decomposed and analyzed under conditions identical with those employed for the trans-1-pyrazoline (XII) no cyclopropane was detected. In order to clarify the question as to whether, in this case, no cyclopropane is formed or whether the cyclopropane formed has an extremely long retention time, one of the isomeric cis-cyclopropanes (XI) was synthesized and analyzed by gas chromatography. The synthesis of the cis-cyclopropane (XI) was accomplished by the methylation of a half-ester obtained by refluxing the cyclopropane anhydride (XV)



XIV

XV



XI

in methyl alcohol. The cyclopropane anhydride (XV), on the other hand, was prepared from the decomposition of pyrazoline anhydride (XIV) resulting from the addition of phenyldiazomethane to citraconic anhydride. When the cyclopropane thus obtained was analyzed by gas chromatography under the condition described previously, it showed a peak with a retention time of 17.7 min.

This observation suggested that probably no cyclopropane was formed under the conditions employed for the decomposition of the cis-1-pyrazoline (X). Attempts were made, therefore, to find conditions under which the cis-1-pyrazoline (X) would yield cyclopropane. The pyrazoline was decomposed at several different temperatures ranging from 140°C. to 260°C. The decompositions were also tried by refluxing the pyrazoline in xylene, mesitylene and decalin. In no case could a cyclopropane be detected in the v. p. c. chart. However, when the cis-pyrazoline (X) was introduced into a test tube preheated at 280-290°C., the decomposition gave cyclopropane.\*

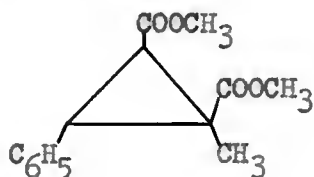
The analysis of the above decomposition product by gas chromatography revealed two peaks, the larger peak with a retention time of 17.7 min. and the smaller peak with a retention time of 12.7 min. The retention time of the large peak was identical to that of the cis-cyclopropane (XI) and the retention time of the small peak to that of the trans-cyclopropane (XIII).

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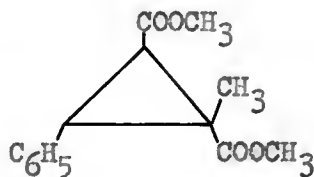
\*When the crude cis-pyrazoline (X) with m.p. 104°C. was melted, the intensity of the -NH absorption in the infrared spectrum increased. It is, therefore, thought that the failure of the formation of the cyclopropane from the cis-pyrazoline (X) with d.p. 137°C. decomposed at the temperature below 260°C. is due to its tautomerization to a 2-pyrazoline, thus preventing the formation of a cyclopropane.

Addition of previously prepared cis- and trans-cyclopropane (XI) and (XIII) to the reaction mixture enhanced the peaks already present, thus confirming the assignment of these peaks to cis- and trans-cyclopropane. Quantitative analysis by gas chromatography revealed that the decomposition product of the cis-pyrazoline (X) contained approximately 6 percent of cis-cyclopropane (XI) and approximately 2 percent of trans-cyclopropane (XIII), indicating the decomposition was stereoselective regarding the cis- and trans-relationship of the two carbomethoxy groups.

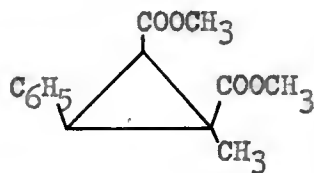
It now becomes necessary to consider the stereochemistry about the third and remaining carbon atom in the cyclopropane ring. There are four possible isomeric cyclopropanes (XVI), (XVII), (XVIII) and (XIX) which can be derived from the 1-pyrazolines (X) and (XII). Of these four cyclopropanes, the ones with structures (XVIII) and (XIX) are sterically less



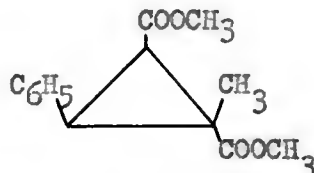
XVI



XVII



XVIII

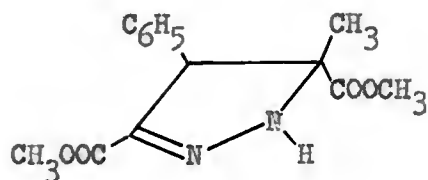


XIX

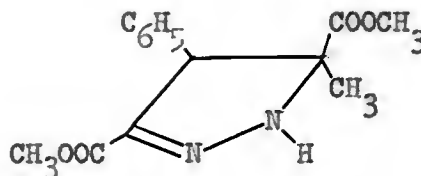
stable than the ones with structures (XVI) and (XVII), due to the fact that there are three bulky groups on the same side of the cyclopropane ring. Actually only two cyclopropanes were detected from the decomposition

products of the 1-pyrazolines (X) and (XII). It was, therefore, reasoned that the cyclopropanes resulted from the decomposition of cis- and trans-1-pyrazolines were most likely the sterically more favorable cyclopropanes (XVI) and (XVII).

In order to verify the above stereochemical assignments, the two 2-pyrazolines (XX) and (XXI) were prepared by reactions of methyl diazoacetate with methyl  $\alpha$ -methyl cinnamate and methyl allo- $\alpha$ -methyl cinnamate respectively. The decomposition of these 2-pyrazolines was effected at 200-250°C.



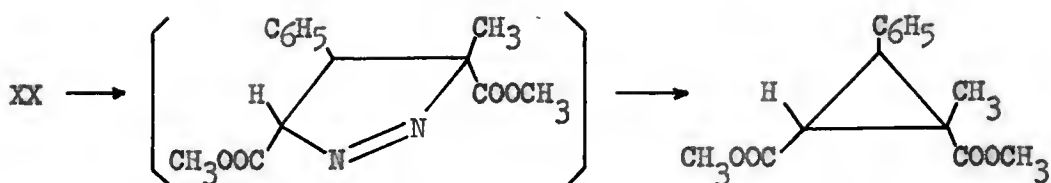
XX



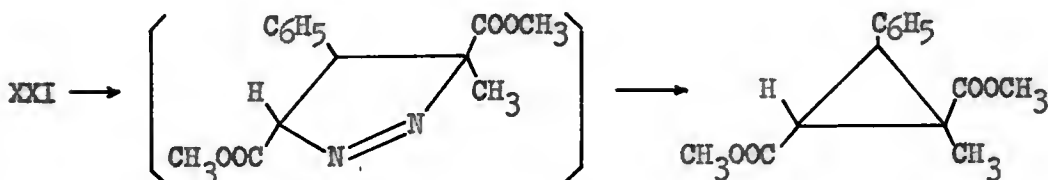
XXI

According to Jones, the stereochemical course of the decomposition of 2-pyrazolines can be predicted by presuming that the reaction proceeds by an initial tautomerization to the sterically favored 1-pyrazoline followed by expulsion of nitrogen.<sup>5,6</sup> This rule has been confirmed for certain 3-carbomethoxy-2-pyrazolines. Since both 2-pyrazolines (XX) and (XXI) are 3-carbomethoxy-2-pyrazolines, upon decomposition they could be expected to yield predominately cis- and trans-cyclopropane (XVI) and (XVII) respectively.

The results of the analyses of the decomposition products of 2-pyrazolines (XX) and (XXI) by gas chromatography were in line with the expectations. The analysis of the decomposition product of 2-pyrazoline



XVI



XVII

(XX) indicated that the decomposition product contained a maximum of 79 percent by weight of the cis-cyclopropane (XI) and a maximum of 8 percent by weight of the trans-cyclopropane (XIII) (or other material with similar retention time). The results of the analysis of the decomposition products of the 2-pyrazoline (XXI), on the other hand, indicated that the decomposition product contained a maximum of 23 percent by weight of the trans-cyclopropane (XIII) and a maximum of 9 percent by weight of the cis-cyclopropane (XI) (or other material with similar retention time). The major cyclopropanes in the decomposition products of the 2-pyrazolines (XX) and (XXI) were both isolated by liquid phase chromatography and confirmed by their infrared spectra to be identical with cis- and trans-cyclopropanes (XI) and (XIII) respectively.

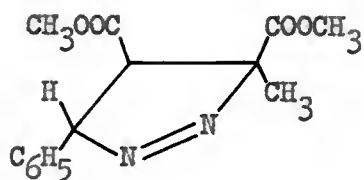
The fact that the two 2-pyrazolines which were decomposed gave different major cyclopropane products is a good indication that at no time during the decomposition did equilibrating rotation around the single bonds occur. Thus, the stereochemical relationship of the phenyl and the ring-

methyl must be the same in the product as in the reactant. If this is true, then the fact that the cyclopropanes resulting from the decomposition of the 2-pyrazolines are identical with those resulting from the decomposition of the 1-pyrazolines leads to the conclusion that cyclopropanes resulting from the decomposition of cis- and trans-1-pyrazolines actually have the structure pictured in XVI and XVII, respectively.

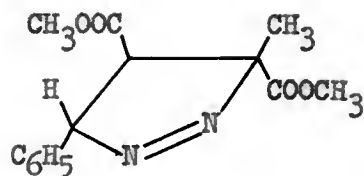
The n.m.r. analyses also confirmed the above stereochemical assignments for the cyclopropane (XI) and (XIII). The results of analysis showed that the cis-cyclopropane (XI) had a coupling constant of 6.9 c.p.s. and the trans-cyclopropane (XIII) 7.2 c.p.s. for the two neighboring cyclopropane hydrogens, demonstrating that in both cyclopropanes the two hydrogen atoms were in the trans configuration.<sup>7</sup>

The consideration of the stereochemistry of the cyclopropanes assigned above suggested that the phenyl groups on the C-5 atom of the original 1-pyrazolines (X) and (XII) were trans to the carbomethoxy groups on the C-4 atom of the pyrazolines. As the hydrogen atoms in the cyclopropanes found in the decomposition product were trans with respect to one another, it seems likely that the two hydrogen atoms in the parent pyrazolines also assume the same stereochemistry. Otherwise, the decomposition of the pyrazolines (X) and (XII) would require that there were only equilibration between the C-4 and the C-5 atom and no equilibration between the C-3 and the C-4 atom of the pyrazolines taking place.

For this reason the structures (XXII) and (XXIII) are assigned for the pyrazolines (X) and (XII) respectively. However, the assignments are not very conclusive in view of the possibility that the rotation around



XXII



XXIII

the bonds between the C-4 and the C-5 atom could conceivably be easier than those between the C-3 and the C-4 atom of the pyrazolines due to the presence of the bulky methyl group (or the carbomethoxy group for the pyrazoline (XII)) on the C-3 atom as compared to the small hydrogen atom on the C-5 atom of the pyrazoline.

### III. EXPERIMENTAL

Preparation of 3-methyl-cis-3,4-dicarbomethoxy-5,5-diphenyl-1-pyrazoline (V). — To 10 grams (0.0556 mole) of dimethyl citraconate<sup>8</sup> was added 10.8 grams (0.0556 mole) of crystalline diphenyldiazomethane obtained from the oxidation of benzophenone-hydrazone.<sup>9</sup> The resultant solution was set aside with occasional shaking. After two days, the whole solution had solidified. The solidified mass was pink colored. After one week, the slightly pink mass was filtered and the resulting solid was washed twice with 50 ml. portions of ether and then recrystallized three times from methyl alcohol to give 8.4 grams of coarse colorless crystals; m.p. 124°C. with decomposition.<sup>4</sup> Yield: 43.0 percent.

Analysis: Calculated as  $C_{20}H_{20}O_4N_2$ : C, 68.18; H, 5.68; N, 7.95.

Found: C, 67.81; H, 5.95; N, 8.08.

The infrared spectrum indicated the absence of the -NH group.

Decomposition of 3-methyl-cis-3,4-dicarbomethoxy-5,5-diphenyl-1-pyrazoline (V). — A sample (0.237 gram; 0.673 mmoles) of V was decomposed at 125°C. until nitrogen evolution had ceased. The decomposition product, white solid, weighed 0.217 gram (equivalent to 0.670 mmole of the corresponding cyclopropane (VI)). Recrystallization of the product from methyl alcohol yielded colorless needles, m.p. 114-115°C., which did not decolorize  $KMnO_4$  solution.<sup>4</sup> Admixture with the decomposition product from the trans-pyrazoline (VII) showed no depression in melting point. Infrared spectra of the two decomposition products were also identical.

Preparation of 3-methyl-trans-3,4-dicarbomethoxy-5,5-diphenyl-1-pyrazoline (VII). -- To 10 grams (0.0556 mole) of dimethyl mesaconate<sup>10</sup> was added 10.8 grams (0.0556 mole) of diphenyldiazomethane.<sup>9</sup> The resultant solution was shaken well and set aside overnight. By the next morning, the whole solution had solidified. The solidified mass was slightly pink colored. After one week all of the pink color had disappeared. The greenish solid left behind was then washed with ether and recrystallized from methanol to yield 9.1 grams of coarse crystals; m.p. 104°C. with decomposition. Yield: 46.4 percent.

Analysis: Calculated as  $C_{20}H_{20}O_4N_2$ : C, 68.18; H, 5.68; N, 7.95.

Found: C, 68.28; H, 5.71; N, 8.22.

The infrared spectrum indicated the absence of the -NH group.

Decomposition of 3-methyl-trans-3,4-dicarbomethoxy-5,5-diphenyl-1-pyrazoline (VII). -- A sample of 0.192 gram (0.546 mmole) of VII was decomposed at 105°C. until nitrogen evolution had ceased. The decomposition product, white solid, weighed 0.177 gram (corresponding to 0.545 mmole of 1-methyl-trans-1,2-dicarbomethoxy-3,3-diphenyl cyclopropane (VI)). Recrystallization of the product from methyl alcohol yielded colorless crystalline; needles, m.p. 115°C., which did not decolorize  $KMnO_4$  solution. Admixture with the decomposition product from 3-methyl-cis-3,4-dicarbomethoxy-5,5-diphenyl-1-pyrazoline (V) showed no depression in melting point. The infrared spectra of the two decomposition products were also identical.

Preparation of benzaldehyde-hydrazone. -- To an ice-cooled solution of anhydrous hydrazine (64.0 grams, 2.00 moles) was added dropwise with stirring a solution of 106 grams (1.00 mole) of benzaldehyde in 300 ml.

of ether. After the addition of the benzaldehyde solution, the resultant solution was dried over solid sodium hydroxide for three or four days until the solution became reddish brown. The solution was then filtered and the solvent and excess hydrazine were removed on a water bath under the vacuum of a water aspirator. The residue was distilled at a pressure of 12 mm. Seventy-two grams of the distillate with b.p. 134-136°C. were obtained. Yield: 60.0 percent. (Different preparations resulted in different yields which ranged from 58.3 to 61.3 percent.)

Preparation of phenyldiazomethane. — Fifty grams (0.458 mole) of benzaldehyde-hydrazone was suspended in 500 ml. of pentane. With stirring 100 grams (0.463 mole) of red mercuric oxide were introduced to the suspension in a time interval of two and one-half hours. After the addition of mercuric oxide the reaction mixture was further stirred for one-half of an hour. The mixture was then filtered to remove insoluble materials. The residue was washed with 50 ml. of pentane. The washing was combined with the filtrate. The final volume of the pentane solution was 530 ml.

From titration with maleic anhydride, the concentration of phenyldiazomethane in pentane was estimated to be  $0.313 \times 10^{-4}$  mmole/ml. Yield: 37.8 percent.

Preparation of 3-methyl-cis-3,4-dicarbomethoxy-5-phenyl-1-pyrazoline (X). —

To 14.8 grams (0.0939 mole) of dimethyl citraconate was slowly added 300 ml. of ice-cold solution of pentane containing 11.1 grams (0.0939 mole) of phenyldiazomethane. The resultant solution was shaken well and was placed in the refrigerator. After three days at this temperature, a mass of white solid contaminated with orange and yellow precipitates had formed.

The solids were filtered and washed several times with pentane until the washing was only slightly yellow. The solid was then washed with ether to remove the remaining yellow color in the white solid. The white solid after washing and drying in a vacuum desiccator weighed 18.40 grams, m.p. 104-109°C. The white solid was unstable in the air. Upon standing in the air for three or four hours the solid changed to a brownish viscous mess. It was also unstable in warm methanol, chloroform and carbon tetrachloride solution. When the white solid, m.p. 104-109°C., was dissolved in any of these solvents the solution changed from colorless to yellow.

The white solid with m.p. 104-109°C. (15.65 grams) was dissolved in approximately 800 ml. of ether. After most of the solvent was removed by the slow evaporation of ether in the hood, the colorless crystals formed were separated from the remaining yellow oil by filtration. The colorless crystals after being washed with ether weighed 3.05 grams, m.p. 130°C. with decomposition. The white crystals (1.47 grams), m.p. 130°C. with decomposition, were recrystallized from cold methanol solution to yield 1.30 grams of the white crystals, m.p. 137°C. with decomposition. Yield: 12.1 percent.

Analysis: Calculated as  $C_{14}H_{16}N_2O_4$ : C, 60.90; H, 5.80.

Found: C, 60.93; H, 5.83.

The infrared spectrum indicated the absence of the -NH group.

Preparation of 3-methyl-trans-3,4-dicarbomethoxy-5-phenyl-1-pyrazoline

(XII). -- To 24.50 grams (0.155 mole) of dimethyl mesaconate was slowly added 218 ml. of ice-cooled solution of pentane containing 18.3 grams

(0.155 mole) of phenyldiazomethane. The resultant solution was shaken well and placed in the refrigerator.

After three days, a mass of white solid contaminated with orange and yellow precipitates deposited on the bottom of the flask. The solids were filtered, washed several times with pentane until the washing solution was only slightly yellow. The solids were further washed with ether to give 38.5 grams of white solid which melted at  $63^{\circ}\text{C}$ . (started to bubble at  $65^{\circ}\text{C}$ .).

Ten grams of the white solid with m.p.  $63^{\circ}\text{C}$ . were dissolved in approximately 50 ml. of ether and the solution was placed in the refrigerator. After about a week, the white solid which had separated was filtered and recrystallized from acetone. M.p.  $175^{\circ}\text{C}$ . with decomposition. Yield: 1.1 grams (9.9 percent).

Analysis: Calculated as  $\text{C}_{14}\text{H}_{16}\text{N}_2\text{O}_4$ : C, 60.90; H, 5.80; N, 10.14.

Found: C, 61.02; H, 5.69; N, 10.08. C, 61.15; H, 5.79; N, 10.22.

Infrared absorptions indicated the absence of the -NH group.

In some cases, even after weeks in the refrigerator, the reaction product of dimethyl mesaconate and phenyldiazomethane failed to solidify. In these cases, the two layers formed in the flask were separated. An approximately equal volume of ether was added to the reddish viscous oil that had been the bottom layer, and the ether was slowly evaporated at ice temperature for several days. The white solid separated was recrystallized from acetone to give a white solid which decomposed at  $175^{\circ}\text{C}$ .

In a typical run, 300 ml. of pentane containing 0.111 mole of phenyldiazomethane were added to 18.7 grams (0.111 mole) of dimethyl mesaconate

and 3.2 grams (yield: 10.4 percent) of the white solid with decomposition point 175°C. were isolated by the afore-mentioned method.

Preparation of 1-methyl-cis-1,2-dicarbomethoxy-3-phenylcyclopropane (XI). —

To thirty grams (0.268 mole) of citraconic anhydride was added an equimolar amount of phenyldiazomethane in 500 ml. of pentane. The reaction mixture was set in the ice room. The next day, 33.3 grams of white solid contaminated with a small amount of yellow crystals had formed. The solid was isolated, dried in the vacuum desiccator and decomposed at 90-100°C. The decomposed product weighed 28.8 grams. Twelve grams of the decomposition product was refluxed in 150 ml. of 95 percent methanol solution for 6 hours. After refluxing the solvent was removed on the water bath under the vacuum of a water aspirator. To the residue an ethereal solution of diazomethane was added until bubbles were no longer evolved. The ether was removed and the residue was dissolved in acetone and oxidized with 10 percent  $\text{KMnO}_4$  solution. The brown and black precipitates formed during the course of the oxidation were filtered. Water was added to the filtrate and the resultant solution was extracted three times with 20 ml. portions of ether. The ether extracts were combined and dried over anhydrous calcium sulfate. After the removal of ether the residue was distilled. The fraction which distilled at 160-162°C./6 mm. was collected. Yield: 3.2 grams (11.6 percent).

Analysis: Calculated as  $\text{C}_{14}\text{H}_{16}\text{O}_4$ : C, 67.78; H, 6.45.

Found: C, 67.62; H, 6.72.

NMR Analysis: Coupling constant for neighboring hydrogen atoms; 6.9

c.p.s.

Isolation of 1-methyl-trans-1,2-dicarbomethoxy-3-phenylcyclopropane

(XIII). -- The oil (43.2 grams) resulting from the preparation of trans-pyrazoline (XII) was fractionally distilled to give the following fractions.

Fraction	B. P. °C.	P. mm.	Wt. gr.
1	104-120	15	3.0
2	120-120	15	1.1
3	160-160	13	0.5
4	160-175	13	1.2
5	175-190	13	14.0
Residue			22.0

One gram of the distillate from the fifth fraction was chromatographed by using a column (diameter, 1.5 cm.; length, 30 cm.) packed with 40 grams of acid-washed alumina. The sample was transferred into the column by dissolving in a very small amount of 35 percent ether in hexane. Twenty percent ether in hexane was used as eluent. The following fractions were collected.

Fraction	Volume, ml.	Wt. of the residue, mg.
1	70	35
2	50	20
3	60	123
4	30	134
5	30	98
6	35	100
7	50	21

The residue from fractions 2-7 were dissolved in hexane and cooled at 0°C. over night to give 320 mg. of white precipitate. Recrystallization of the white precipitate several times from MeOH-H<sub>2</sub>O yielded 250 mg. of colorless crystals, m.p. 41.5-43°C., which did not decolorize KMnO<sub>4</sub> solution. Yield: 28.4 percent.

Analysis: Calculated as C<sub>14</sub>H<sub>16</sub>O<sub>4</sub>: C, 67.78; H, 6.45.

Found: C, 68.16; H, 6.49.

NMR Analysis: Coupling constant for neighboring hydrogen atoms; 7.2 c.p.s.

Hydrolysis of trans-cyclopropane (XIII). -- A sample of 0.65 grams of the trans-cyclopropane was dissolved in 5 ml. of 5 percent KOH-MeOH solution. After 4 days, the above solution was poured into 20 ml. of distilled water and acidified with 10 percent HCl solution until the solution was strongly acidic. The solution which became turbid was then extracted three times with ether. The ether extracts were combined, washed with distilled water until the washings were neutral to litmus paper. The ether solution was dried over anhydrous calcium sulfate over night. The residue obtained after the removal of ether weighed 0.54 grams m.p. 104-110°C. Recrystallization from MeOH-H<sub>2</sub>O yielded colorless crystals with m.p. 113-115°C. Yield: 93 percent.

Analysis: Calculated as C<sub>12</sub>H<sub>12</sub>O<sub>4</sub>: C, 65.5; H, 5.46.

Found: C, 65.75; H, 5.64.

A small amount of the di-acid was converted to its dimethyl ester with diazomethane.<sup>11</sup> Its infrared spectrum, melting point, and mixed melting point with pure trans-cyclopropane proved that no isomerization had occurred during the hydrolysis. An attempt to close the di-acid to

the anhydride failed. Upon heating the acid at 200-230°C. and 30 mm. in a sublimation apparatus, only unchanged acid sublimed, m.p. 113-115°C. Mixed with pure acid; no depression in melting point.

Preparation of 3,5-dicarbomethoxy-4-phenyl-5-methyl-2-pyrazoline with phenyl and methyl groups cis (XX). -- To 24.1 grams (0.137 mole) of methyl  $\alpha$ -methylcinnamate<sup>12</sup> was added 13.70 grams (0.137 mole) of methyl diazoacetate<sup>13</sup> prepared from the diazotization of methyl glycinate hydrochloride.<sup>14</sup> The resultant yellow solution was heated at 90-95°C. for 3 days. The completion of the reaction was tested by addition of a few drops of dilute hydrochloric acid solution to a small portion of the reaction mixture. No nitrogen evolution was observed. The reaction mixture was then eluted with ether through a column (diameter, 3 cm.; length, 50 cm.) packed with 200 grams of acid-washed alumina. The residue obtained after the evaporation of ether weighed 33.0 grams. A 17.4 grams portion of the residue was distilled under nitrogen at a pressure of 4.9 mm. to remove unreacted methyl  $\alpha$ -methylcinnamate. The fractions which distilled up to 160°C. were collected. The residue remaining in the distillation pot weighed 8.1 grams. The residue was recrystallized from CCl<sub>4</sub> to give 2.35 grams of colorless crystals of m.p. 113-116°C. Repeated recrystallization from CCl<sub>4</sub> yielded white crystals, m.p. 114.5-115°C. Yield: 11.8 percent.

Analysis: Calculated as C<sub>14</sub>H<sub>16</sub>O<sub>4</sub>N<sub>2</sub>: C, 60.90; H, 5.80; N, 10.14.

Found: C, 60.91; H, 5.97; N, 10.20.

Significant infrared absorptions: 2.95, 5.71, 5.81, 6.41 microns.

Preparation of 3,5-dicarbomethoxy-4-phenyl-5-methyl-2-pyrazoline with phenyl and methyl groups trans (XXI). -- To 2.93 grams (0.0176 mole) of methyl allo- $\alpha$ -methylcinnamate<sup>15</sup> was added 1.76 grams (0.0176 mole) of methyl diazoacetate. The resultant solution was heated at 80-85°C. for 4 days. At the end of this time a small portion of the reaction mixture gave no nitrogen evolution upon the addition of dilute hydrochloric acid solution. The solution was then distilled at a pressure of 5 mm. to remove unreacted methyl allo- $\alpha$ -methylcinnamate. All material which boiled up to 106°C. (2.24 grams) was collected. The residue in the distillation pot, weighed 1.75 grams. Significant infrared absorptions: 2.99, 5.70, 5.80, 6.15, 14.25 microns. Without further purification the residue was decomposed and the decomposition product analyzed by gas chromatography.

General procedure for gas chromatographic analysis of the decomposition product. -- A Perkin Elmer Model 154-B vapor fractometer, operating at 188-192°C. and 25 p.s.i. and utilizing an 18-foot coiled 1/4 inch copper tube packed with 30-60 mesh Tide detergent (F & M Scientific Corp.) was employed for analyses of the decomposition products.

Before the column was used for analysis, it was "baked" in the heating chamber for about 18 hours at a temperature of 180-190°C. and a helium pressure of 10 p.s.i. to remove excess liquid phase from the detergent packing. The liquid phase comes off initially in a discontinuous fashion, finally leveling off to a constant flow which continues throughout the operational life of the column. If not removed prior to the column's use, this initial effluent causes an erratic pattern of thermistor response which interferes with the analysis.

The column was standardized by preparing separately samples of the two isomeric cyclopropanes and 4-t-butylcyclohexanone (used as an internal standard) of known concentrations and calculating the areas of the peak on the v.p.c. chart for from four to ten injections for each sample. Plots of each area vs. number of micromole of sample were then constructed from these results. Reasonably good straight line relationships of the peak area vs. number of micromole of samples were obtained (Figures 1, 2, and 3).

In analyzing the reaction products a weighed amount of 4-t-butylcyclohexanone was added to a given amount of the decomposition product. The mixture was dissolved in chloroform solution and was analyzed by gas chromatography. The area ratio of 4-t-butylcyclohexanone to cyclopropanes was measured and their mole ratio found from the standard curves. From the weights of 4-t-butylcyclohexanone and the decomposition product, and their mole ratio, the weight percentage of the cyclopropane in the decomposition product was calculated.

In cases of analyses for the decomposition products of the 2-pyrazolines (XX) and (XXI), it was found that the cis- and trans-cyclopropane peaks were not cleanly separated. In order to solve this difficulty the following approximation was used: the line was extended along the curve on the v.p.c. chart and the area under the peak was measured to estimate the maximum percentage of the cyclopropane as illustrated in Figure 4.

Under the experimental conditions (temperature 188-192°C., 25 p.s.i. and utilizing an 18-foot column, etc.) the retention times of trans- and

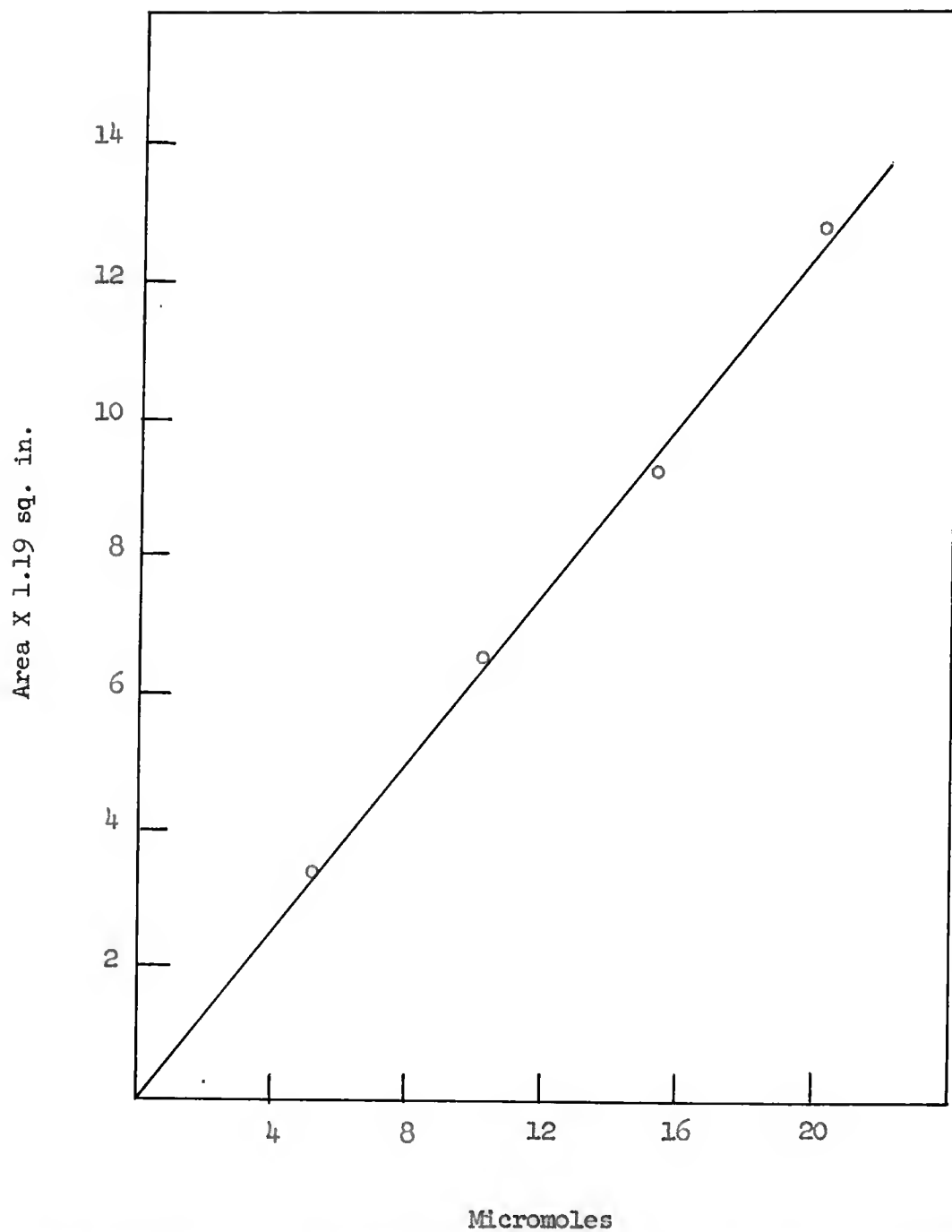


Figure 1. -- The standarization curve for the cis-cyclopropane (XVI).

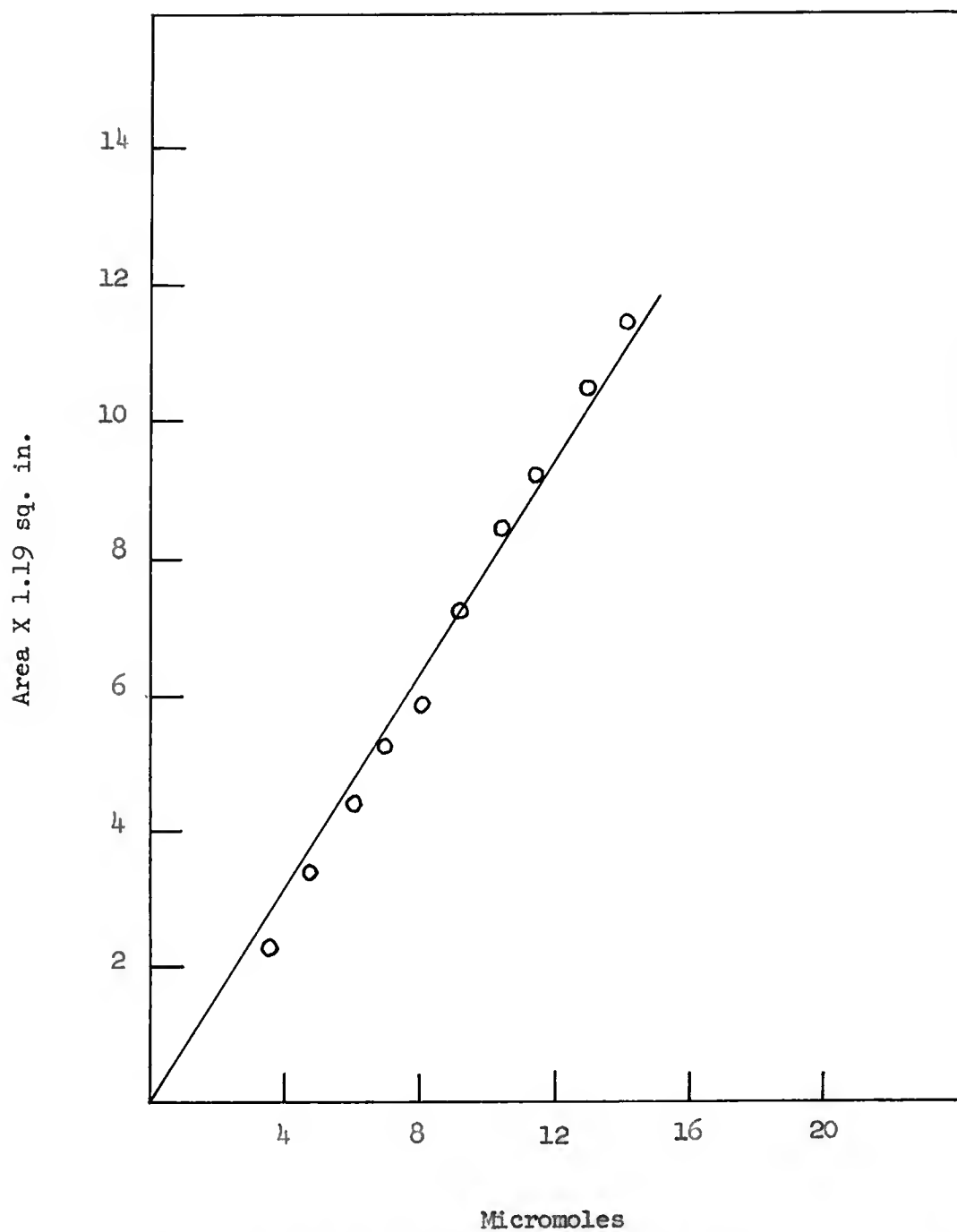


Figure 2. — The standarization curve for the trans-cyclopropane (XVII).

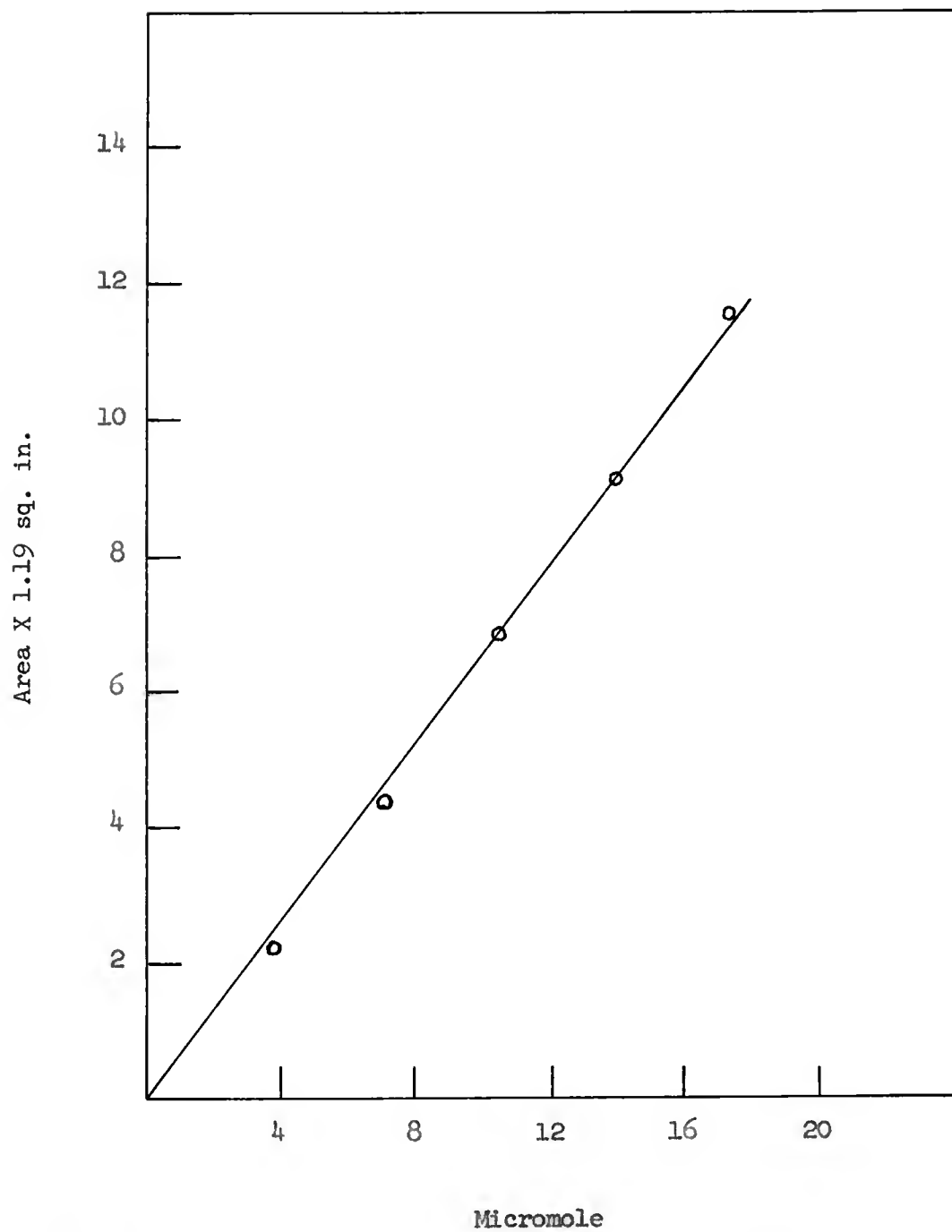


Figure 3. -- The standarization curve for 4-t-butylcyclohexanone.

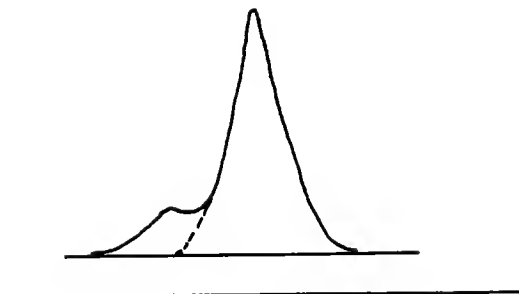


Figure 4. — An illustration for the estimation of the max. peak area.

cis-cyclopropanes ranged from 13 to 16 min. and 15 to 18 min. respectively. For this reason when the decomposition products were analyzed for qualitative purposes, pure trans- and cis-cyclopropane were added to a portion of the product to ensure the correctness of the results of the analyses.

Decomposition of 3-methyl-cis-3,4-dicarbomethoxy-5-phenyl-1-pyrazoline (X). —

No cyclopropane was formed when the cis-pyrazoline (X) was decomposed at several different temperatures ranging from 140 to 260°C. Refluxing the cis-pyrazoline (X) in xylene, mesitylene and decalin also did not give cyclopropane. However, when the pyrazoline was decomposed at 280-290°C., it was decomposed to yield cyclopropane.

A sample of 0.240 grams of the cis-pyrazoline (X) with d.p. 137°C. was introduced in a test tube preheated at 280-290°C. The residue weighed 0.180 grams. From the analysis by gas chromatography, the residue was found to contain approximately 6 percent by weight of the cis-cyclopropane (XI) and approximately 2 percent by weight of the trans-cyclopropane (XIII).

Gas chromatographic analysis.

Wt. of the decomposition product	180.0 mg.
Wt. of 4- <u>t</u> -butylcyclohexanone	14.0 mg.

Area ratio:

<u>cis</u> -cyclopropane to 4- <u>t</u> -butylcyclohexanone	0.439
<u>trans</u> -cyclopropane to 4- <u>t</u> -butylcyclohexanone	0.014

Mole ratio:

<u>cis</u> -cyclopropane to 4- <u>t</u> -butylcyclohexanone	0.469
<u>trans</u> -cyclopropane to 4- <u>t</u> -butylcyclohexanone	0.116

Wt. percentage:

<u>cis</u> -cyclopropane	5.9
<u>trans</u> -cyclopropane	1.5

It was further observed that under the above experimental condition the mole ratio of cis- to trans-cyclopropane products was not independent of the purity, as indicated by the melting point of the cis-1-pyrazoline. The mole ratio of cis : trans cyclopropane was observed to be 9.4 : 0.2 when the decomposition point of the cis-1-pyrazoline was 133°C.; 8 : 1 when the melting point was 104°C.; and as previously described, 6 : 2 when the decomposition point was 137°C.

Decomposition of 3-methyl-trans-3,4-dicarbomethoxy-5-phenyl-1-pyrazoline (XII). -- A sample of 0.0823 grams of the trans-pyrazoline (XII) was decomposed at 180-185°C. The residue weighed 0.0784 grams. From the analysis by gas chromatography, the residue was found to contain approximately 12 percent of the trans-cyclopropane (XIII). No detectable amount of the cis-cyclopropane (XI) could be found. The cis-cyclopropane (XI) was also found to be absent in the decomposition product of the crude reaction mixture of the trans-pyrazoline (XII).

Gas chromatographic analysis.

Wt. of the decomposition product 137.1 mg.

Wt. of 4-t-butylcyclohexanone 25.1 mg.

Area ratio:

trans-cyclopropane to 4-t-butylcyclohexanone 0.513

Mole ratio:

trans-cyclopropane to 4-t-butylcyclohexanone 0.513

Wt. percentage of the cyclopropane 12.2

Decomposition of the 2-pyrazoline (XX). — A sample of 0.617 grams of the 2-pyrazoline (XX) was decomposed at 240-260°C. until 53.30 ml. (at 753 mm. and 28°C.) of nitrogen had been evolved. The analysis of the decomposition product by gas chromatography showed it to contain a maximum of 78.5 percent by weight of the cis-cyclopropane (XI) and a maximum of 8.4 percent by weight of the trans-cyclopropane (XIII). Due to the presence of an uncharacterized impurity in the decomposition product the peaks of the cis- and the trans-cyclopropane were not cleanly separated. Therefore, the approximation described in "General Procedure for Gas Chromatographic Analysis of the Decomposition Product" was employed to estimate the maximum percentage by weight of the two cyclopropanes in the decomposition product.

The major cyclopropane product, the cis-cyclopropane, was isolated from the decomposition product by liquid phase chromatography by using acid-washed alumina as an adsorbent and 20 percent ether in pentane as an eluent. The infrared spectrum of the isolated cyclopropane was identical to that of the cis-cyclopropane (XI).

Gas chromatographic analysis.

Wt. of the decomposition product 22.8 mg.

Wt. of 4-t-butylcyclohexanone 5.1 mg.

Area ratio:

cis-cyclopropane to 4-t-butylcyclohexanone 2.10

trans-cyclopropane to 4-t-butylcyclohexanone 0.28

Mole ratio:

cis-cyclopropane to 4-t-butylcyclohexanone 2.22

trans-cyclopropane to 4-t-butylcyclohexanone 0.24

Wt. percentage:

cis-cyclopropane 78.5

trans-cyclopropane 8.4

Decomposition of crude 2-pyrazoline (XXI). — A sample of 1.19 grams of crude XXI was decomposed at 200-250°C. until 89.80 ml. (at 759.7 mm. and 25°C.) of nitrogen had been evolved. The decomposition product weighed 0.94 grams. The decomposition product was analyzed by gas chromatography and the presence of both trans- and cis-cyclopropane were confirmed. However, quantitative evaluation of the cis- and trans-cyclopropane presented two difficulties. First, under the experimental conditions employed, the cyclopropane peaks were not cleanly separated to allow accurate determinations. Second, there was a peak with a retention time very close to that of the internal standard, 4-t-butylcyclohexanone. The last difficulty was overcome by the following method: the area ratio of the trans-cyclopropane to the interferring peak was determined. From this ratio, the area of the trans-cyclopropane peak and the sum of the areas of

the internal standard and interfering peaks, the area of the interfering peak was calculated and eliminated. The approximation method described in "General Procedure to Gas Chromatographic Analysis of the Decomposition Product" was used to overcome the first difficulty. In this way the maximum weight percents of trans- and cis-cyclopropanes were estimated to be 22.6 percent and 8.8 percent respectively.

The major cyclopropane product, the trans-cyclopropane, was isolated from the decomposition product (0.80 gram) by liquid phase chromatography by using acid-washed alumina (17 grams) as an adsorbent and 20 percent ether in hexane as an eluent. The residue (ca. 0.10 gram) obtained after the evaporation of the solvent from the first four fractions (total volume, 99 ml.) was confirmed to be trans-cyclopropane by comparison of its infrared spectrum with that of trans-cyclopropane (XIII).

Gas chromatographic analysis.

Wt. of the decomposition product	49.0 mg.
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Wt. of 4- <u>t</u> -butylcyclohexanone	76.9 mg.
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Area ratio:

<u>cis</u> -cyclopropane to 4- <u>t</u> -butylcyclohexanone	0.196
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plus interfering peak

<u>trans</u> -cyclopropane to 4- <u>t</u> -butylcyclohexanone	0.578
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plus interfering peak

<u>trans</u> -cyclopropane to interfering peak	1.38
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Mole ratio:

<u>cis</u> -cyclopropane to 4- <u>t</u> -butylcyclohexanone	0.354
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<u>trans</u> -cyclopropane to 4- <u>t</u> -butylcyclohexanone	0.812
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Wt. percentage:

<u>cis</u> -cyclopropane	8.8
<u>trans</u> -cyclopropane	22.6

#### IV. SUMMARY

The non-stereospecificity of the decomposition of 3-methyl-cis-3,4-dicarbomethoxy-5,5-diphenyl-1-pyrazoline (V) reported by van Alphen has been confirmed by the comparison of the decomposition of his pyrazoline with that of isomeric 3-methyl-trans-3,4-dicarbomethoxy-5,5-diphenyl-1-pyrazoline (VII). Both pyrazolines decomposed to give the same product.

3-Methyl-cis-3,4-dicarbomethoxy-5-phenyl-1-pyrazoline (XXII) and 3-methyl-trans-3,4-dicarbomethoxy-5-phenyl-1-pyrazoline (XXIII) have been synthesized and the stereochemistry of the phenyl groups in these pyrazolines has been tentatively assigned as trans to the carbomethoxy group on the C-4 atom of the pyrazolines.

The decomposition of the cis-1-pyrazoline (XXII) yielded 6 percent by weight of the cis-cyclopropane (XVI) and 2 percent by weight of the trans-cyclopropane (XVII), while the decomposition of the trans-1-pyrazoline (XXIII) gave 12 percent by weight of the trans-cyclopropane (XVII) and no detectable amount of the cis-isomer, indicating that the decompositions in these cases are stereoselective.

The geometrical configurations of the cyclopropanes resulting from the decomposition of the 1-pyrazolines have been assigned as a result of synthesis of the cyclopropane with cis-carboalkoxy groups from the anhydride, stereospecific syntheses of each cyclopropane from appropriate 2-pyrazolines and attempted anhydride formation from the di-acid resulting

from hydrolysis of XIII. The assigned configurations have been further confirmed by n.m.r. analyses.

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## BIOGRAPHICAL SKETCH

Wun-Ten Tai was born January 24, 1932, in Taipei, Taiwan. He entered the National Taiwan University, Taipei, Taiwan, in September, 1950, and graduated in June, 1954, with the degree of Bachelor of Science. After serving one year as a full time teaching assistant at the National Taiwan University, he entered the Graduate School of the University of South Carolina in September, 1956, and graduated in August, 1958, with the degree of Master of Science.

In September, 1956, Mr. Tai entered the Graduate School of the University of Florida. He held a graduate assistantship until June, 1960, and the remainder of his work was supported by a National Science Foundation grant.

Mr. Tai is married and the father of one child. He is a member of Gamma Sigma Epsilon.


This dissertation was prepared under the direction of the chairman of the candidate's supervisory committee and has been approved by all members of that committee. It was submitted to the Dean of the College of Arts and Sciences and to the Graduate Council, and was approved as partial fulfillment of the requirements for the degree of Doctor of Philosophy.

June 5, 1961

  
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Dean, College of Arts and Sciences

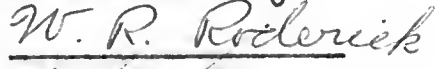
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